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Original Research Article

Survival outcomes of parotid carcinomas treated with surgery and adjuvant radiation therapy

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ABSTRACT

Background: Parotid cancers are a diverse histological group of cancers involving the parotid gland with varying effects of prognostic factors on treatment outcomes. The effect of adjuvant radiotherapy on the outcome in parotid cancers has always been debated in the past. The objective of current study was to measure the effect of prognostic factors and the survival outcomes of patients with primary parotid cancers treated with surgery and adjuvant radiotherapy.
Methods: From January 2010 to December 2023, a total of 61 patients treated at Freeman Hospital, were included in the analysis. Data was collected and stratified according to age, gender, tumour staging, surgical margins, lymphovascular invasion (LVI), peri-neural invasion (PNI), extra nodal extension (ENE) and recurrence rate. All patients treated with surgery and adjuvant radiotherapy were included in the study. Patients with incomplete data, distant metastasis or those lost to follow up were excluded. The OS, DSS and RFS rates based on surgical margins, LVI, PNI and ENE were calculated.
Results: The 5-year OS, DSS and RFS were 72.6%, 79.6% and 77.7%, respectively. Positive surgical margins did not influence the survival outcome in comparison to close or clear margins. Lower survival rates were noted for patients with ENE, although not reaching statistical significance.
Conclusion: Though retrospective in nature, our study provides valuable information that close or involved surgical margins do not adversely affect the outcome for parotid cancers treated with surgery and adjuvant radiotherapy and that surgical re-resection might not be indicated in this patient population.

Keywords: Parotid carcinoma, Surgery, Radiotherapy, Surgical margins, Survival, Recurrence

INTRODUCTION

Salivary gland neoplasms are relatively rare, representing only 2% of all head and neck malignancies. This group of cancers constitute a wide range of histological subtypes, with varied tumour biology and behaviour. Among salivary gland neoplasms, parotid gland tumours represent the most common primary site of malignant tumours despite higher malignant to benign ratio found in other salivary glands.[1] The variation of tumour characteristics and scarcity of cases can pose challenges in evidence-based treatment decision making. Difficulties with inaccurate pre-operative diagnosis from Fine Needle Aspiration cytology (FNAC) is unfortunately a common occurrence, resulting in an un-expected pathological diagnosis of malignancy following resection of a perceived benign salivary tumours.[2] Whilst open biopsy and core biopsy may offer more accurate pre-treatment pathological information, the risk of tumour seeding or facial nerve injury often means surgical excision is planned to confirm diagnosis.[3] It is ideal to preserve a functioning facial nerve in all types of parotid surgery and the balance between margin status and nerve preservation often falls on the side of nerve preservation,

especially when there has not been pre-operative confirmation of malignancy. In these circumstances revision surgery to improve margin status remains an option, although it carries significant risk of morbidity, particularly with regards to facial nerve function. Adjuvant radiotherapy is routinely employed in high-risk cases.

Evidence exists that tumour grading and staging as well as histological sub-types can affect the outcomes in parotid malignancy. Additionally, the effect of adverse pathological features such as surgical margin status, lympho-vascular invasion (LVI), perineural invasion (PNI) and extranodal extension (ENE) have been evaluated in previously published studies to assess their prognostic implications, with variable outcomes.[3] Previous studies have demonstrated the combined effect of these factors on the outcome, with limited data assessing the adverse pathological features independently. Our study focused on the individual effect of these factors on the survival outcomes for parotid malignancies.

The primary objective of current study was to measure the survival outcomes of patients with primary parotid carcinoma treated with surgery and post operative radiotherapy. The secondary objective was to evaluate the effect of certain prognostic factors on survival outcomes.

METHODS

For this retrospective study, institutional database was searched for the patients with parotid carcinoma treated with surgery and adjuvant radiotherapy over a period of 14 years (from January 2010 to December 2023). Patients with primary parotid carcinoma treated with surgery and adjuvant radiotherapy were included in the analysis. Patients with benign tumours, salivary gland subsites other than parotid gland, presence of distant metastases at the time of diagnosis were excluded. A total of 61 patients met the inclusion criteria and were included in the analysis.

Data collection included gender, age, histological sub-types, tumour staging and types of parotid surgeries performed with a particular focus on margin status. Surgical margins less than 1 mm from tumour resection were considered to be involved, while margins between 1-5 mm from resection margin were defined as close margins. Clear tumour margins were more than 5mm from the resection. The details on neck dissections (selective, modified or radical) were also collected and presence or absence of LVI, PNI and ENE were also recorded for all patients.

Patients' survival outcomes included overall survival (OS), disease-specific survival (DSS) and recurrence-free survival (RFS). Time-to-event was measured in months from the date of diagnosis. Patients were censored at the date of last follow-up or at the time of death from causes unrelated to the primary malignancy, where applicable.

Statistical analysis

Kaplan–Meier (KM) survival analysis was performed to estimate survival rates for the entire cohort and for subgroups stratified by the presence or absence of margin status, LVI, PNI and ENE. Comparisons between survival distributions were conducted using the log-rank test. Five-year survival probabilities and associated 95% confidence intervals (CIs) were calculated using Greenwood's formula.

All statistical analyses and visualisations were performed using R version 4.4.0 (R Core Team, 2025). KM estimation and log-rank testing were carried out using the survival package, while survival curves were visualised using the survminer package. Additional data wrangling and formatting were performed using dplyr and ggplot2.

RESULTS

Demographic and diagnostic information

Of the total of 61 patients included in the review, 35 were males and 26 were females. The median age of whole cohort was 65.5 years (range 26–89). Histological variants included adenocarcinoma, which was the most prevalent subtypes present in 33 (54%) patients, followed by acinic cell carcinoma in 9 (14.8%) patients. Mucoepidermoid, squamous cell carcinoma and adenoid cystic carcinomas were less prevalent. As per the AJCC TNM 8th edition, stage IV was the most common stage, 26 patients (42.6%) followed by stage II disease present in 17 (27.9%) patients, stage III in 12 (19.7%) and stage I in 6 (9.8%) respectively (Table 1).

Surgical procedures

Regarding surgery, partial parotidectomy was the most common procedure performed, which was in 22 (36.1%) patients, followed by superficial parotidectomy, performed in 19 (31.1%) patients. Total parotidectomy was performed in 15 (24.6%) patients and 5(8.2%) patients underwent radical parotidectomies. Of a total 61 patients, 43 (70.5%) underwent neck dissection; 33 (54.1%) patients had selective neck dissection and 10 (16.4%) patients had modified radical neck dissection.

Pathological characteristics

Concerning surgical excision margins, 19 (31.1%) patients had clear margins, 24 (39.4%) patients had close margins and in remaining 18 (29.5%) patients, there were involved margins. Nodal disease was present in 19 (31.1%) patients of which ENE was noted in 11 (18% of the total 61 patients). LVI and PNI were present in 20 (32.8%) and 21 (34.4%) patients, respectively. Disease recurred in 15 (24.6%) patients, with 8 (12.9%) patients

having distant metastasis, the rest being loco-regional recurrence (Table 2).

Survival by surgical margins

The results for OS and DSS f or resection margins, interestingly, showed clear margins exhibiting lower OS and DSS compared to those with close or involved margins. The five-year OS was 45.2% for clear margins, compared to 79.8% and 87.5% for close and involved margins, respectively (p=0.67). Similarly, the five-year DSS for the clear margin group was 61.2% versus 83.6% and 87.5% in the close and involved groups (p=0.43). The five-year RFS estimates were 65.5% for clear margins, 81.5% and 80.8% for close and involved margins (p=0.212) (Figure 1).

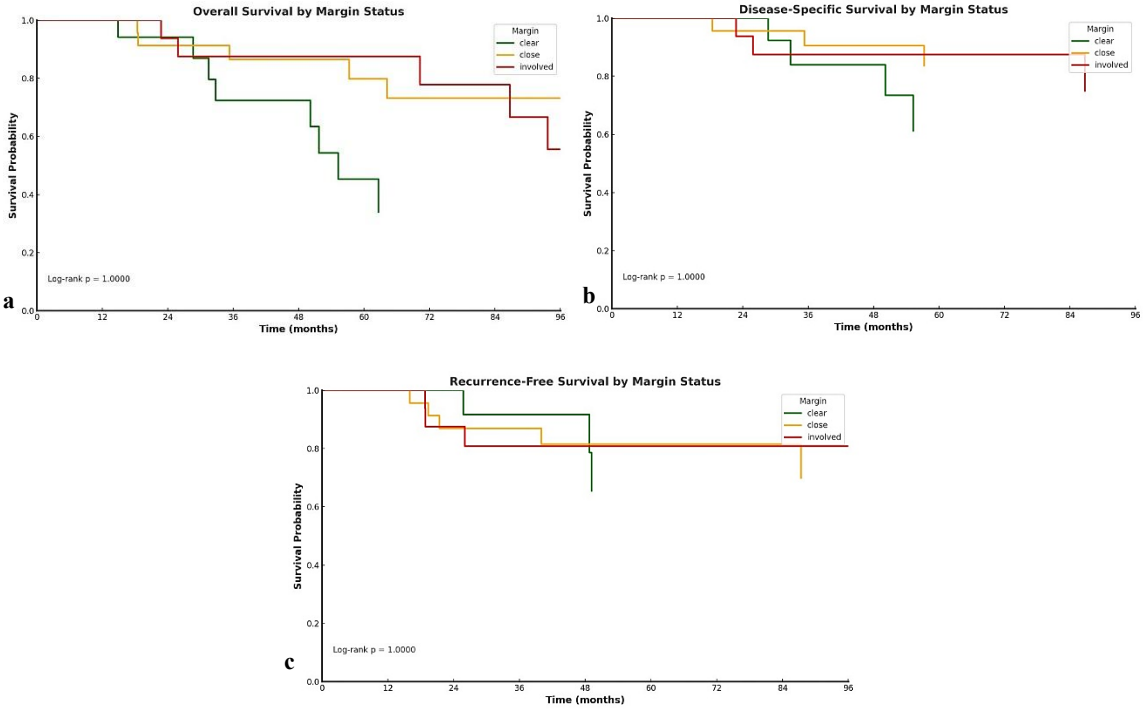

Figure 1 (a-c): Survival outcomes in relation to surgical margins.

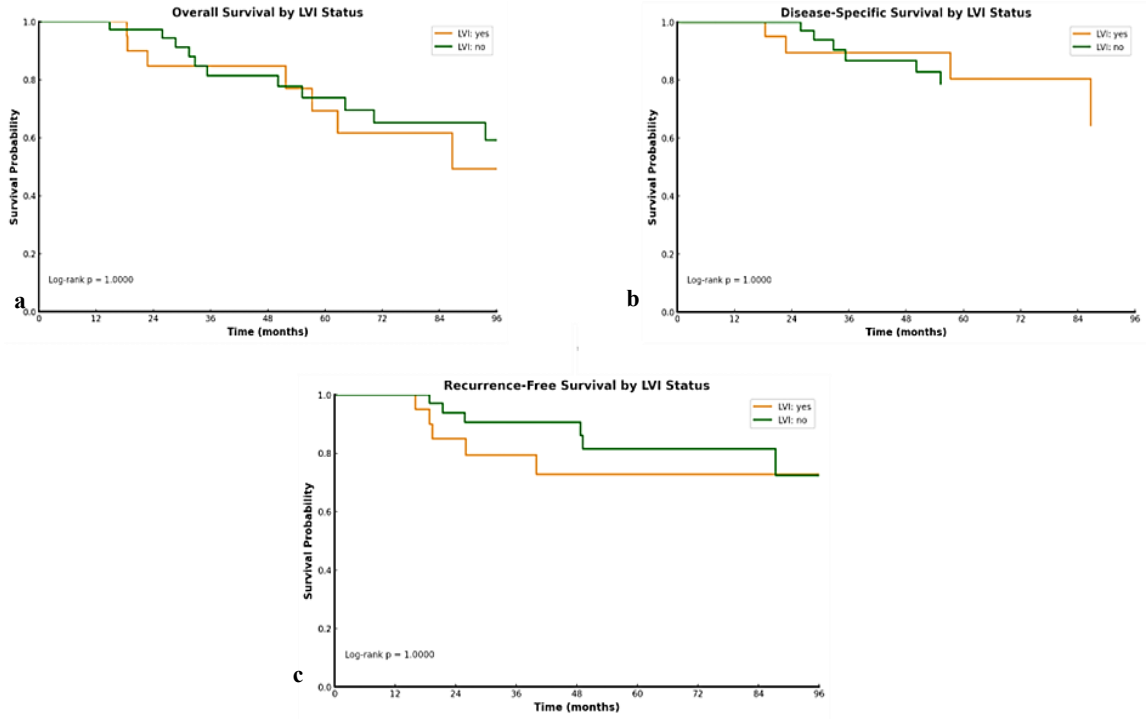

Figure 2 (a-c): Survival outcomes in relation to LVI.

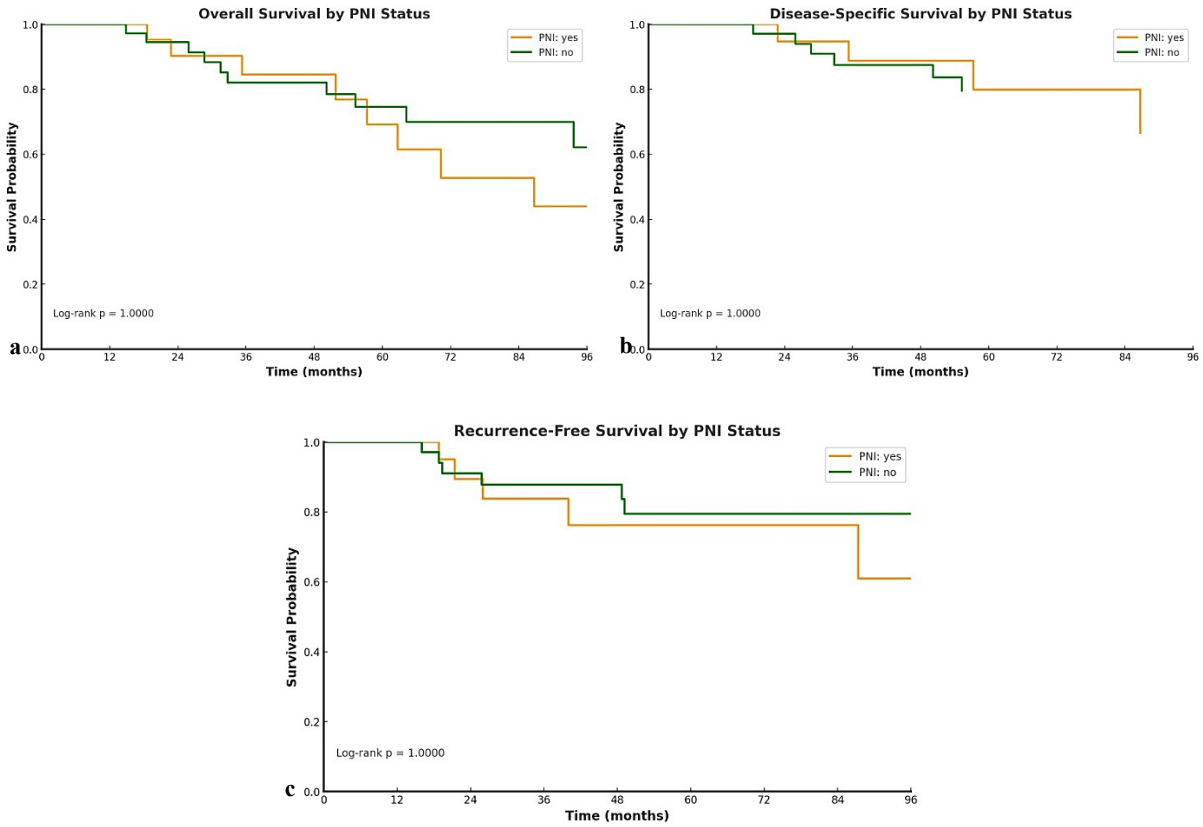

Figure 3 (a-c): Survival outcomes in relation to PNI.

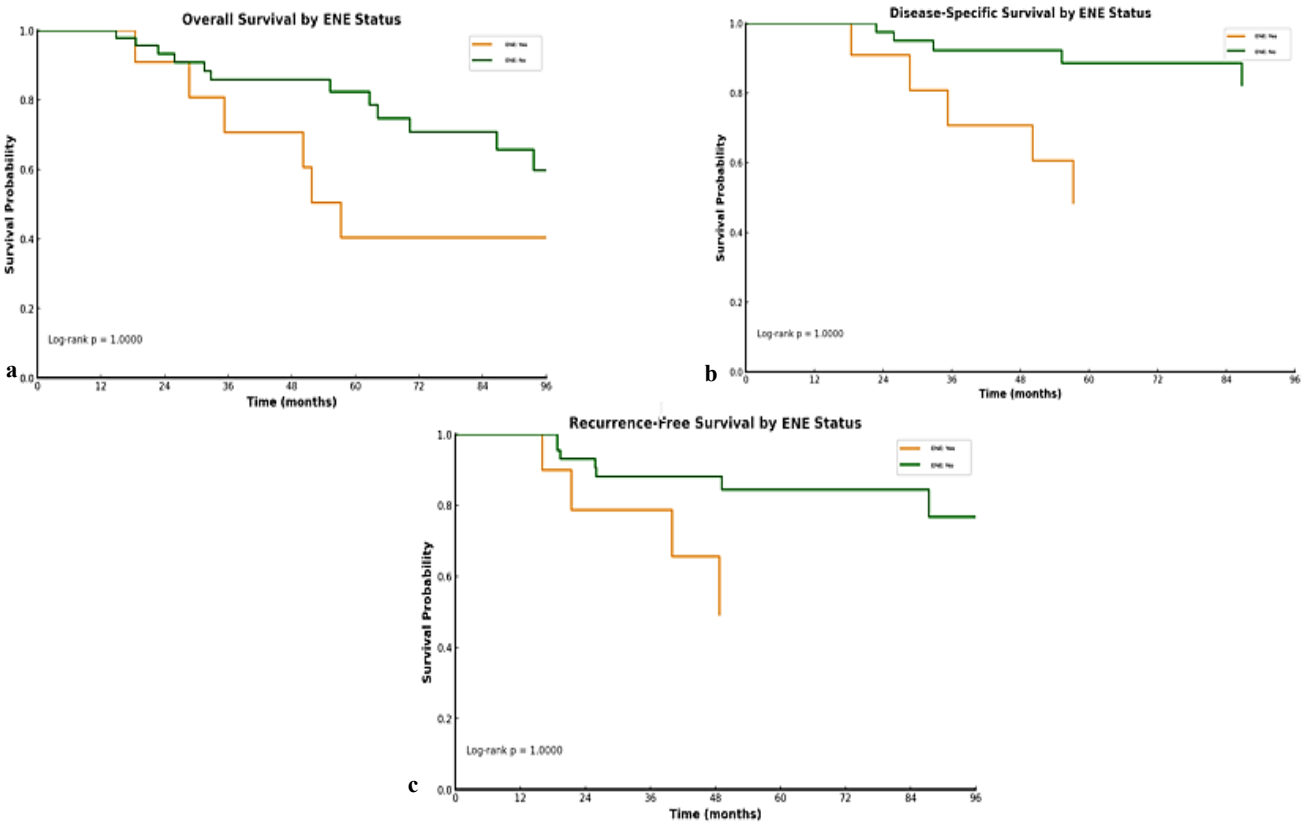

Figure 4 (a-c): Survival outcome in relation to extranodal extension.

Survival by lympho-vascular invasion

There was no significant change noted in any of the survival outcomes of patients with positive LVI in comparison to negative LVI. This was demonstrated in the five-year OS rates which was 69.3% for LVI positive patients versus 73.8% for LVI-negative patients (p=0.747).

Additionally, the five-year DSS and RFS estimates also showed no significant difference in the survival outcomes, with DSS in LVI positive patients being 80.5% and 78.7% for LVN negative patient (p =0.98) and RFS for LVI positive patients being 81.5% and 72.7% for LVI negative patient (p=0.625) (Figure 2).

Survival by perineural invasion

There was no significant difference noted in the five-year survival outcomes of patients with PNI patients and PNI negative patients. Five-year OS was 69.2% in PNI positive patients, whereas it was noted to be 74.5% in PNI negative patients, with a p value of 0.799. Both the five-year DSS and RFS rates were almost similar for PNI positive and PNI negative patients. The DSS rates were 79.9% and 79.5% for PNI positive versus PNI negative patients respectively (p= 0.924), while the RFS rates were 76.2% for PNI positive and 79.5% for PNI negative patients with a p value of 0.807 (Figure 3).

Survival by extranodal extension

There were clinically meaningful reductions in all survival endpoints for patients with ENE, even though not statistically significant. The five-year OS in ENE patients was 82.4%, with a noticeable reduction in the OS for ENE positive patients to 40.4% (p=0.132). The five-year DSS trends followed a similar pattern with a survival outcome reducing from 88.6% for ENE positive to 48.5% for ENE negative patients (p=0.070). There was also an obvious reduction in the survival rates for ENE positive patients and ENE negative patients, with the values being 49.2% and 84.4% but again with no statistical difference (p=0.103) (Figure 4).

Overall survival outcomes

In the overall cohort, the estimated five-year OS was 72.6%. The five-year DSS and RFS were 79.6% and 77.7%, respectively.

Table 1: Demographic and clinicopathologic characteristics of whole patient cohort.

Characteristics	N (%)
Gender	
Male	35 (57.3)
Female	26 (42.7)
Age (in years)	
Median age	65.5
Range	26-89
Histology	
Adenocarcinoma	33 (54)
Acinic cell	9 (14.8)
Mucoepidermoid	5 (8.2)
Adenoid cystic	3 (5.0)
SCC	5 (8.2)
Others	6 (9.8)
Overall Staging	
I	6 (9.8)
II	17 (27.9)
III	12 (19.7)
IV	26 (42.6)

Table 2: Pathological characteristics and outcomes.

Pathological characteristics	N (%)
LVI	
Yes	20 (32.8)
No	41 (67.2)
PNI	
Yes	21 (34.4)
No	40 (65.6)
ENE	
Yes	11 (18)
No	50 (82)

Continued.

Pathological characteristics	N (%)
Margins	
Clear	19 (31.1)
Close	24 (39.4)
Involved	18 (29.5)
Recurrence	
Yes	15 (24.6)
No	46 (75.4)

DISCUSSION

Parotid malignancies constitute a heterogeneous group of cancers, with diverse biological behaviours and variation in outcomes, but with similar management strategies. Identification of adverse clinical prognostic factors aids decision making particularly when considering adjuvant therapy after surgery.[4,5] Previous studies have examined the implication of adverse prognostic features in salivary cancers, however, there are limited studies which focus on individualized effect of adverse pathological features such as LVI, PNI, ENE and surgical margins.

The study showed a wide variation in age ranging from 26 years to 89 years of age, with a median age of 65.5 years. Majority of patients presented after 50 years of age, with males being slightly more commonly affected then females. Published data in the past have indicated that most parotid malignancies frequently present between the fourth to seventh decades of life with a male preponderance, although there have been some studies mentioning females being more commonly affected with malignant parotid tumours.[6-8]

Mucoid epidermoid carcinoma is considered the commonest parotid malignancy, accounting for 10-15% of salivary gland malignancies.[9] Interestingly our data showed a higher incidence of high-grade adenocarcinoma. Acinic cell carcinoma was the second most common variant. This could be explained by selection bias in our study which focused upon patients treated with surgery followed by adjuvant radiotherapy, considering as many patients with low-grade muco-epidermoid carcinoma are likely to be managed with surgery alone.[10,11] Whilst there are many factors that are known to affect the outcome in parotid malignancies, we specifically focused on the effect of surgical margins on outcomes, for patients treated with surgery and radiotherapy. Other prognostic factors for instance LVI, PNI and ENE were also looked into as independent prognostic factors.

Whilst there are many factors that are known to affect the outcome in parotid malignancies, we specifically focused on the effect of surgical margins. The definition of involved margins is not standardized, but in most cases is considered the same as for oral cavity tumours. As per Müller et al, we deemed surgical margins less than 1mm as involved, between 1-5 mm as close and more than 5mm as clear margins.[12] The implication of a positive resection margin on outcomes shows a lack of concordance in the literature. Morse et al noted a strong negative impact on OS and DSS with positive margins but no difference in RFS.[13] In contrast, other studies report no difference in survival outcome based on surgical margins.[14] Similarly, Gutschenritter et al concluded that the positive, close or involved margins had no effect at all on survival outcomes, further acknowledging it as an unexpected finding. There is some debate in the literature that adjuvant radiotherapy after surgery can offer good survival outcomes despite positive or close margins, a finding supported by our data as well.[15,16] Lin et al included 101 patients in their study receiving adjuvant radiotherapy after surgery and the authors concluded that clinical outcomes for patients with positive margins were equal to those with clear margins.[17]

Given the differing conclusions in the literature, clinical decision making of whether to offer adjuvant treatment or re-operation to improve margin status in the context of an incomplete resection should be guided by synthesis of this data. Our data supports the notion that the effect of adjuvant radiotherapy negates the impact of close or positive margins, since excellent control outcomes can be achieved by adjuvant radiotherapy. Furthermore, this strategy avoids the potential morbidity of revisions surgery, particularly relevant to facial nerve function.

Many studies highlighted the intricate association of LVI and PNI and considered them strong predictors of distant metastasis and survival.[18,19] Ouyang et al reported that LVI was a strong independent factor affecting survival and recurrence in parotid cancers. They further recommended risk-adapted follow up strategies, with enhanced clinical follow up in patients with LVI.[20] In the study, LVI was present in 20 patients and there was a trend towards lower RFS, although not statistically significant. This could be due to a small sample size, one of the limitations of this study.

PNI is the histological infiltration of tumour into the nerve and is one of the factors that advocates the need for multimodal treatment. It is quite prevalent in salivary gland malignancies, being present in up to 40% of patients. Huyett et al, in their case series of 186 patients, mentioned worse OS and RFS in patients with PNI, though statistically insignificant when other prognostic factors were also considered.[1] In contrast, Katabi et al found similar OS, DSS and RFS between patients with and without PNI.[21] Kazemian et al recently published a meta-analysis of 14 studies which have overall indicated

PNI as a worse prognostic factor for salivary gland malignancies. They have noted variations in conclusions due to difference in sample sizes and considerations of different prognostic factors in each study, along with the PNI.[22] Authors noted 21 patients in the study to have PNI, with a lower survival trend for OS, DSS and RFS, though again not statistically significant.

In the AJCC TNM 8th edition, the nodal classification for salivary gland malignancies was revised to include ENE as part of the classification. This has also proved to be beneficial in looking at survival outcomes with the burden of ENE in parotid malignancies.[23] In the analysis, out of the 19 patients with positive nodal disease, ENE was present in 11 patients. OS, DSS and RFS rates were all noticeably reduced in the presence of ENE. Published studies identify ENE as an adverse prognostic factor with greater negative impact upon survival than involved resection margins for certain histological variants. Lee et al concluded that ENE was an independent prognostic indicator for recurrence and survival outcomes.[24] Conversely, other studies negate the role of ENE in survival outcomes, highlighting ongoing controversy in this area.[25,26] Whist data from further prospective studies are needed to robustly scrutinize the impact of ENE on survival in salivary malignancies, the data presented here highlights adverse outcomes following treatment when ENE is present.

The limitation of this study mainly relates to small sample size and the retrospective nature of this analysis. Care was taken to ensure rigorous scrutiny of the data available for the included patients, resulting in a number being excluded from statistical analysis when datapoints such as pathological information was not available. Authors acknowledge that the absence of a control group for comparison would have been ideal, however the intention was to focus upon the impact of adverse pathological features when adjuvant therapy was planned and feel that the data would have been skewed by including highly selected, low-grade and low-risk malignancies where the intention was to treat with surgery alone.

CONCLUSION

The single institutional study over a period of 14 years' time span provides valuable information on this relatively rare tumour site. It supports the concept of adjuvant radiotherapy over re-operation when adequate margins are not achieved. It also highlights poorer survival outcomes for patients with extranodal extension. Given the rarity of disease, large multi-institutional prospective studies are required to confirm the findings and to guide decision making in future.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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